Rosa canina L. Methanol Extract and Its Component Rutin Reduce Cholesterol More Efficiently than Miglustat in Niemann–Pick C Fibroblasts

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Abstract

Niemann–Pick type C (NPC) disease is an autosomal recessive lysosomal storage disorder where 95% of the cases are caused by mutations in the Niemann–Pick C1 (NPC1) gene. Loss of function in NPC1 mutants trigger the accumulation of cholesterol in late endo-lysosomes and lysosomal dysfunction. The current study examined the potential of polyphenol-rich methanol extracts from Rosa canina L. (RCME) and two of its components, rutin and quercitrin, to enhance protein trafficking of NPC1 and restore cholesterol levels in fibroblasts derived from NPC patients, in comparison with miglustat, a drug approved in Europe for NPC treatment. Interestingly, RCME improved the trafficking of the compound heterozygous mutant NPC1I1061T/P887L, homozygous mutant NPC1R1266Q, and heterozygous mutant NPC1N1156S between the endoplasmic reticulum and the Golgi and significantly reduced the levels of cellular cholesterol in the cell lines examined. Miglustat did not affect the trafficking of the three NPC1 mutants individually nor in combination with RCME. Markedly, rutin and quercitrin exerted their effects on cholesterol, but not in the trafficking pathway of NPC1, indicating that other components in RCME are implicated in regulating the trafficking of NPC1 mutants. By virtue of its dual function in targeting the trafficking of mutants of NPC1 as well as the cholesterol contents, RCME is more beneficial than available drugs that target substrate reduction and should be therefore considered in further studies for its feasibility as a therapeutic agent for NPC patients.